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Is the weekend effect true in acute stroke patients at tertiary stroke center?

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ABSTRACT

Background: There is contradicting evidence on the outcome of emergency patients treated during weekends versus weekdays. We studied if outcome of ischemic stroke patients receiving intravenous thrombolysis (IVT) differs according to the treatment time.

Methods: Our retrospective study included consecutive patients receiving IVT within 4.5 h of stroke onset between June 1995 and December 2018 at the Helsinki University Hospital. The patients were compared based on the treatment initiation either during weekdays (Monday to Friday) or weekend (Saturday and Sunday). The primary outcome was 3-month mortality and secondary outcomes comprised 3-month modified Rankin Scale (mRS) and incidence of symptomatic intracerebral hemorrhage (sICH). Additional analyses studied the effect of IVT treatment according to non-office hours, time of day, and season.

Results: Of the 3980 IVT-treated patients, 28.0% received treatment during weekends. Mortality was similar after weekend (10.0%) and weekday (10.6%) admissions in the multivariable regression analysis (OR 0.78; 95% CI 0.59–1.03). Neither 3-month mRS (OR 0.98; 95% CI 0.86–1.12), nor the occurrence of sICH (4.2% vs 4.6%; OR 0.87; 95% CI 0.60–1.26) differed between the groups. No outcome difference was observed between the office vs non-office hours or by the time of day. However, odds for worse outcome were higher during autumn (OR 1.19; 95% CI 1.04–1.35) and winter (OR 1.15; 95% CI 1.01–1.30).

Conclusion: We did not discover any weekend effect for IVT-treated stroke patients. This confirms that with standardized procedures, an equal quality of care can be provided to patients requiring urgent treatment irrespective of time.

1. Introduction

The so-called weekend effect, a poorer outcome for patients admitted to hospital at weekends, has been rigorously investigated without reaching a final conclusion. Although the phenomenon itself has emerged in several meta-analyses [1–4], its mechanisms and prevalence among different specialties and hospitals are not well established. A meta-analysis of acute ischemic stroke patients reported increased short-term mortality and poorer functional outcome at discharge after off-hour admission [5], but since then opposing results have also been published [6–8]. Several reasons for the weekend effect has been suggested, such as lower quality of care [9–12], higher case severity [13–15], or different patient flow.

In a recent study from our center, Tolvi et al. reported a weekend effect in several specialties of a major university hospital, including neurology [16]. This finding is in contrast to our earlier study that indicated no association of outcome and admission time among a prominent patient group at the neurological Emergency Department, stroke patients treated with intravenous thrombolysis (IVT) [17].

As any change in quality of care would demand urgent re-evaluation of the standardized procedures, we investigated whether a weekend effect for acute ischemic stroke patients has emerged since our original publication [17]. Additionally, we repeated the analyses of circadian phenomena of IVT outcomes in order to get an updated insight into the level of care for acute stroke patients 24/7.

Abbreviations: EVT, Endovascular thrombectomy; HSQR, Helsinki Stroke Quality register; IVT, Intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Stroke Scale; sICH, symptomatic intracranial hemorrhage.

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2. Material and methods

2.1. Patient selection

We performed a retrospective, single-center analysis from the Helsinki Stroke Quality register (HSQR). HSQR comprises all stroke patients admitted as a neurologic patient to the Emergency Department of the Helsinki University Hospital, the only comprehensive stroke center in the Uusimaa province with a catchment population of approximately 1.6 million. All stroke patients within the area who are candidates for IVT or endovascular thrombectomy (EVT) are admitted to our center. Patients with significant premorbid disability, equating modified Rankin Scale (mRS) score > 2, are usually treated at their local Emergency Department according to the local protocol. HSQR contains data on patient demographics, premorbid cardiovascular diseases and medication, time stamps of symptom onset, admission, and administration of IVT, imaging results, baseline National Institutes of Stroke Scale (NIHSS) score, and clinical outcome at three months.

Our cohort comprised patients treated with IVT during the study years, including those with IVT and subsequent EVT to treat large vessel occlusion. However, patients undergoing direct EVT were excluded from the analyses. The treatment complied with institutional standardized guidelines for acute stroke care, which are updated biannually and whenever new scientific evidence becomes available [18]. During the study period, IVT (0.9 mg/kg alteplase) was delivered $\leq$4.5 h in accordance with the recommendations of the American Stroke Association [19].

The acute stroke code protocol of our center has been developed over years and described previously in detail [20,21]. This 'Helsinki model' provides 24/7 stroke services, including on-call stroke physician, a stroke team, comprehensive imaging (e.g. computed tomography, magnetic resonance imaging, and perfusion imaging), laboratory, and access to EVT. The decision to activate the stroke code is made by the stroke physician who individually evaluates a patient's suitability for IVT after a prenotification from emergency medical services. Outside working hours, three neurologists are on call at 15:30–22:00 on weekdays and 09:00–18:00 on weekends, and two neurologists at 22:00–08:00 and 18:00–09:00, respectively. The number of on-call shifts per physician seldom exceeds one in a week. Similar stroke services were available on weekdays and weekends over the study years, and the catchment area for IVT remained unchanged.

The Helsinki University Hospital granted the research permit for this registry study (HUS/190/2021). As data were collected prospectively as a part of routine clinical care for retrospective analysis, an ethical board review was not required at our institution.

2.2. Outcomes

The primary outcome was all-cause mortality within three months of hospital admission, electronically submitted to our patient record system from the Digital and Population Data Services Agency. The secondary outcome was functional recovery as defined by the full range of scores on a 3-month mRS. [22] The functional outcomes had been obtained by a stroke neurologist based on a phone interview with the patient or their relative combined with a review of the electronic medical records. As a tertiary outcome, we defined the frequency of symptomatic intracranial hemorrhage (sICH) according to the European Cooperative Acute Stroke Study II classification [23].

Outcome events were investigated by the day of the week of IVT initiation in order to explore whether a weekend effect exists in our center for acute ischemic stroke patients. For comparability with previous works, weekend was defined as starting at midnight Saturday morning and ending at midnight on Sunday night, using the time stamp of IVT initiation [16]. Additionally, we replicated our previous analyses using the following definitions: time of day according to six-hour blocks (night: 00:00–05:59; morning: 06:00–11:59; afternoon: 12:00–17:59; evening: 18:00–23:59) and office hours as Monday–Friday 08:00–15:45, excluding public holidays. The four seasons were as follows: winter (December, January, February); spring (March, April, May); summer (June, July, August); autumn (September, October, November).

2.3. Statistical analysis

Quantitative variables are expressed as medians (interquartile ranges) and categorical variables as numbers (percentages). For the primary end point, between-group differences were calculated with the chi-square test of proportions (with a two-sided alpha level of 5%). Odds ratios (ORs) and 95%-confidence intervals (CIs) were obtained with a binary logistic regression analysis. For the secondary outcome mRS, the proportional-odds assumption was tested and met. Therefore, an ordinal logistic-regression model was applied to compare the trial groups across the full range of scores on mRS, with the effect estimate for an improvement of at least 1 point in the score presented as a common OR with a 95% CI [24]. The rate of sICH was analyzed with the same tests as the primary outcome. For each outcome, we selected to the multivariable model the baseline variables that were associated ($P < 0.10$) with the outcome in the univariable analysis.

In addition, we performed a sensitivity analysis to study if the association of outcome and weekend admission changed during the study years by analyzing separately the first 1000 patients (June 1996 – June 2008) and the last 1000 patients (June 2015 –December 2018) of our cohort.

Data were analyzed using the SPSS Statistics software version 25 (IBM Corp, Armonk, NY, USA).

2.4. Data availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

3. Results

A total of 4020 patients were enrolled between June 1995 and December 2018. The functional outcome data were missing from 39 patients and the time stamp of IVT initiation from one patient, who were excluded from the final cohort of 3980. Of those, 424 (10.7%) patients had additional endovascular treatment after IVT. sICH data were available for 3864 patients. We observed 2866 (72.0%) IVT initiations on weekdays and 1114 (28.0%) on weekends. There were 1397 (34.8%) treatments started during office hours and 2583 (64.3%) during non-office hours.

Baseline clinical characteristics of the weekend and weekday groups were similar, except for prior chronic heart failure that was more prevalent in the weekday group (Table 1). Variables associated with mortality, mRS, and sICH rate that were included in the multivariable analysis of each outcome are presented in Table 1.

There was no difference in mortality between weekend (10.0%) and weekday (10.6%) admissions in the univariable (OR 0.83; 95% CI 0.65–1.06; $P = 0.14$) or in the multivariable analysis (OR 0.78; 95% CI 0.59–1.03; $P = 0.08$) (Table 2). Neither was weekend admission associated with a higher 3-month mRS score in the univariable ordinal regression (OR 1.01; 95% CI 0.89–1.15; $P = 0.87$) or after the multivariable adjustments (OR 0.98; 95% CI 0.86–1.12; $P = 0.79$) (Fig. 1, Table 2). The frequency of sICH was similar (OR 0.89; 95% CI 0.62–1.27; $P = 0.52$) on weekends (4.2%) and weekdays (4.6%) also after multivariable adjustments (OR 0.87; 95% CI 0.60–1.26; $P = 0.47$).

Further analyses revealed no difference in mortality between non-office (10.5%) and office-hours (10.2%) admissions either in the univariable (OR 1.04; 95% CI 0.84–1.28; $P = 0.72$) or in the multivariable analysis (OR 0.94; 95% CI 0.74–1.20; $P = 0.63$) (Table 2). The initiation of IVT during non-office hours was associated with a higher mRS score in the univariable analysis (OR 1.16; 95% CI 1.03–1.30; $P = 0.01$), but the

Table 1
Baseline characteristics and their association with mRS, mortality, and sICH.

	Missing	Weekday ($n = 2866$)	Weekend ($n = 1114$)	Higher mRS (P)[a]	Mortality (P)[a]	sICH (P)[b]
Age, years, median (IQR)	0	69 (60–77)	70 (60–77)	**<0.01**	**<0.01**	**<0.01**
Sex, men (%)	0	1700 (56.7)	582 (56.9)	**0.05**	0.43	0.88
NIHSS score, median (IQR)	8	23 (15–40)	23 (15–44)	**<0.01**	**<0.01**	**<0.01**
Door-to-treatment time, min, median (IQR)	12	23 (15–40)	23 (15–44)	**<0.01**	**<0.01**	**0.05**
Onset-to-treatment time, min, median (IQR)	8	120 (85–175)	121 (85–172)	**<0.01**	**<0.01**	**0.02**
Atrial fibrillation, n (%)	0	610 (21.3)	235 (21.1)	**<0.01**	**<0.01**	**0.04**
Hypertension, n (%)	2	1701 (59.4)	653 (58.6)	**<0.01**	**0.01**	**0.05**
Diabetes mellitus, n (%)	0	457 (15.9)	164 (14.7)	**<0.01**	**<0.01**	0.17
Hypercholesterolemia, n (%)	4	1176 (41.1)	446 (40.0)	0.57	0.41	0.32
Chronic heart failure, n (%)	0	246 (8.6)	69 (6.2)	**<0.01**	**<0.01**	0.24
Coronary artery disease, n (%)	4	553 (19.3)	210 (18.9)	**<0.01**	**<0.01**	**0.06**
Myocardial infarction, n (%)	3	303 (10.6)	105 (9.4)	**<0.01**	**<0.01**	0.29
Prior ischemic stroke, n (%)	1	344 (12.0)	109 (9.8)	**<0.01**	**0.05**	0.43
Prior transient ischemic attack, n (%)	3	263 (9.2)	80 (7.2)	0.95	0.75	0.98
Admission oral anticoagulation, n (%)[c]	6	158 (5.5)	60 (5.4)	**<0.01**	**<0.01**	0.87
Admission statin, n (%)	21	903 (31.7)	357 (32.1)	**0.03**	**0.01**	**<0.01**
Admission antithrombotic, n (%)	8	1025 (35.8)	394 (35.5)	**<0.01**	**<0.01**	**0.01**
Admission antihypertensive, n (%)	22	1638 (57.5)	642 (57.9)	**<0.01**	**<0.01**	0.16

The significance level was calculated using ordinal univariable regression for modified Rankin Scale (mRS) score and binary univariable regression for mortality and symptomatic intracranial hemorrhage (sICH) rate defined by the European Cooperative Acute Stroke Study II criteria. P-values <0.1 (bolded) were included in the corresponding multivariable model. IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale. [a]n = 3980, [b]n = 3864, [c]International Normalized Ratio below 1.8 in vitamin K users was a requisite for IVT.

Table 2
Three-month modified Rankin Scale (mRS) score, mortality, and symptomatic intracranial hemorrhage (sICH) rate after intravenous thrombolysis for ischemic stroke according to different time points.

	Higher mRS		**Mortality**		**sICH**	
Thrombolysis initiation time	Ordinal univariable regression	Ordinal multivariable regression	Binary univariable regression	Binary multivariable regression	Binary univariable regression	Binary multivariable regression
Monday	0.92 (0.79-1.07)	0.85 (0.73-1.00)	0.98 (0.73-1.31)	0.93 (0.67-1.30)	0.75 (0.46-1.20)	0.77 (0.48-1.25)
Tuesday	0.99 (0.85-1.16)	1.02 (0.87-1.20)	0.90 (0.67-1.22)	1.00 (0.71-1.39)	1.02 (0.67-1.56)	1.06 (0.68-1.65)
Wednesday	1.00 (0.85-1.16)	1.11 (0.94-1.30)	**1.32 (1.01-1.73)**	**1.44 (1.06-1.97)**	1.23 (0.82-1.84)	1.30 (0.85-1.97)
Thursday	0.97 (0.83-1.13)	1.01 (0.86-1.18)	0.97 (0.73-1.29)	1.01 (0.73-1.39)	1.25 (0.84-1.86)	1.20 (0.79-1.82)
Friday	1.11 (0.96-1.30)	1.05 (0.90-1.23)	1.08 (0.82-1.43)	1.05 (0.76-1.45)	0.95 (0.62-1.46)	0.94 (0.61-1.47)
Saturday	1.00 (0.85-1.18)	1.05 (0.89-1.24)	0.80 (0.58-1.11)	0.77 (0.53-1.12)	0.81 (0.50-1.32)	0.82 (0.50-1.35)
Sunday	1.02 (0.86-1.20)	0.92 (0.78-1.09)	0.95 (0.69-1.29)	0.84 (0.58-1.20)	1.00 (0.63-1.58)	0.94 (0.59-1.51)
Weekend	1.01 (0.89-1.15)	0.98 (0.86-1.12)	0.83 (0.65-1.06)	0.78 (0.59-1.03)	0.89 (0.62-1.27)	0.87 (0.60-1.26)
Non-office hours	**1.16 (1.03-1.30)**	1.09 (0.96-1.22)	1.04 (0.84-1.28)	0.94 (0.74-1.20)	0.97 (0.71-1.33)	0.93 (0.67-1.28)
Autumn	**1.15 (1.01-1.31)**	**1.19 (1.04-1.35)**	0.99 (0.78-1.26)	1.03 (0.78-1.35)	0.94 (0.66-1.35)	0.95 (0.66-1.38)
Spring	**0.83 (0.73-0.94)**	**0.86 (0.76-0.97)**	0.89 (0.70-1.12)	0.94 (0.72-1.23)	0.78 (0.55-1.12)	0.84 (0.58-1.21)
Summer	0.92 (0.81-1.05)	**0.85 (0.75-0.98)**	1.11 (0.88-1.40)	1.07 (0.81-1.39)	1.11 (0.78-1.58)	1.12 (0.78-1.61)
Winter	**1.14 (1.01-1.30)**	**1.15 (1.01-1.30)**	1.03 (0.81-1.30)	0.97 (0.74-1.28)	1.22 (0.87-1.70)	1.12 (0.78-1.59)
Night	1.08 (0.90-1.30)	0.95 (0.78-1.15)	1.04 (0.74-1.47)	0.91 (0.60-1.39)	1.05 (0.63-1.75)	0.82 (0.46-1.47)
Morning	0.95 (0.83-1.07)	1.02 (0.90-1.16)	0.96 (0.75-1.21)	1.00 (0.76-1.32)	0.93 (0.65-1.33)	0.93 (0.64-1.35)
Afternoon	0.93 (0.83-1.04)	0.92 (0.82-1.03)	0.92 (0.74-1.13)	0.95 (0.75-1.21)	0.92 (0.67-1.25)	0.97 (0.70-1.34)
Evening	1.11 (0.99-1.26)	1.11 (0.98-1.26)	1.13 (0.90-1.41)	1.09 (0.84-1.41)	1.16 (0.83-1.61)	1.18 (0.84-1.66)
Missing data, n (%)	0 (0.00)	61 (1.53)	0 (0.00)	34 (0.85)	86 (2.16)	143 (3.59)

Results are presented as odds ratios and 95%-confidence intervals. Multivariable adjustments were done for predictive variables of the given outcome in univariable regression (see Table 1). The definitions of time points are described in the Methods. sICH is defined according to the European Cooperative Acute Stroke Study II classification.

association did not remain after adjustments for confounding factors (OR 1.09; 95% CI 0.96–1.22; $P = 0.19$). The frequency of sICH was similar (OR 0.97; 95% CI 0.71–1.33; $P = 0.84$) during non-office hours (4.4%) and office hours (4.6%) and remained so after multivariable adjustments (OR 0.93; 95% CI 0.67–1.28; $P = 0.65$). Finally, no difference in any of the outcomes was found based on hours of the day (Fig. 1, Table 2).

IVT initiated on Wednesdays was associated with mortality (OR 1.44; 95% 1.06–1.97; $P = 0.02$) (Table 2). Additionally, odds for worse functional outcome were higher during autumn (OR 1.19; 95% CI 1.04–1.35; $P = 0.01$) and winter (OR 1.15; 95% CI 1.01–1.30; $P = 0.04$) and lower during spring (OR 0.86; 95% 0.76–0.97; $P = 0.02$) and summer (OR 0.85; 95% CI 0.75–0.98; $P = 0.02$) (Fig. 1, Table 2). Mortality and occurrence of sICH did not differ between the seasons.

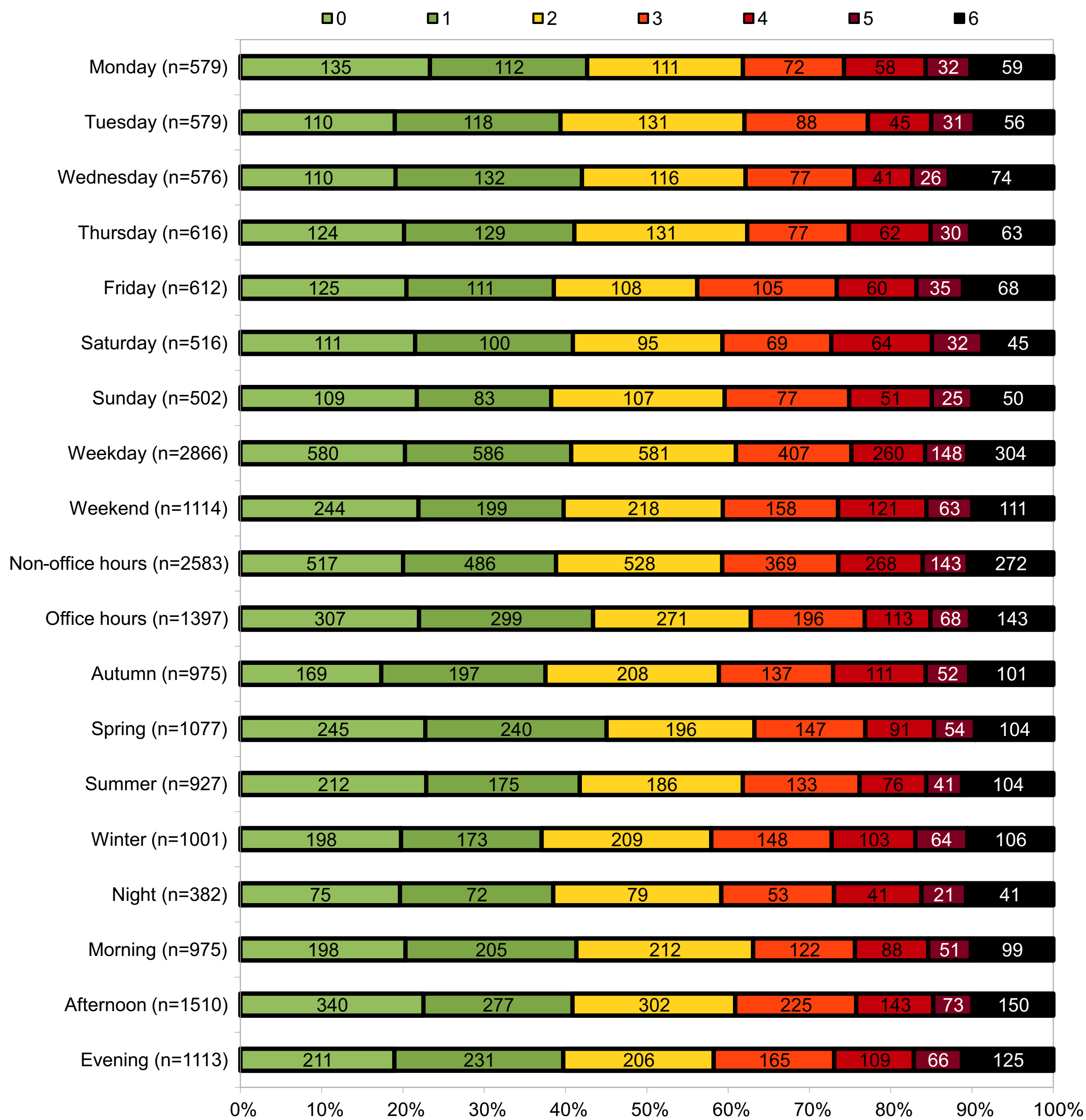

Fig. 1. Three-month modified Rankin Scale (mRS) score after treatment of ischemic stroke with intravenous thrombolysis stratified according to the time point of treatment initiation. Mortality equals an mRS score of 6. The definitions of time points are described in the Methods.

In the sensitivity analyses, mortality did not differ between the patients treated on weekends and weekdays either in the cohort of the first 1000 patients (multivariable OR 0.63; 95% 0.38–1.04; $P = 0.07$) or in the cohort of the last 1000 patients (multivariable OR 0.97; 95% 0.55–1.70; $P = 0.92$). Nor was there difference in the three-month functional outcome among either cohort (first 1000 patients: multivariable OR 0.90; 95% 0.69–1.17; $P = 0.42$; last 1000 patients: multivariable OR 1.04; 95% 0.80–1.34; $P = 0.77$).

4. Discussion

Our results revealed no weekend effect for mortality or functional outcome of acute ischemic stroke patients treated with IVT, 28.0% of which were initiated during weekends. Neither was there difference in outcome for patients treated during office or non-office hours. However, patients admitted during the autumn or winter months achieved poorer functional outcome. The rate of sICH was not associated with the time of IVT initiation.

The results of the present study replicate our previous findings [17] and are in accordance with other studies that have discovered no weekend effect for IVT-treated stroke patients [25–27]. A previous study even found lower mortality for patients receiving IVT on weekends compared to weekdays, in addition to an equal rate of 3-month good functional outcome [28]. Besides weekends, patients treated with IVT during non-office as opposed to office hours seem to have lower short-term mortality [29]. However, previous studies have also reported that patients treated at night have worse functional outcome–a finding that did not appear in our cohort [25,28].

Our steady treatment outcomes might be attributed to the standardized assessment protocol for acute stroke code patients [20,21]. This includes a 24-h access to comprehensive imaging and the presence of a stroke neurologist seven days a week. Consequently, door-to-treatment and onset-to-treatment times in our study were equal among the patients treated on weekends and weekdays, which differs from previous reports of longer treatment delays during weekend admissions [6,28].

Beyond IVT-treated patients, the reasons for the inconsistent results on the weekend effect among stroke patients are not thoroughly understood. The reported IVT rates on weekends have been rather higher [30,31] or equal [25] to weekdays and do not therefore offer an explanation. Other suggestions include differences in stroke services [9], as well as methodological issues, such as adjustment for confounding factors, mainly disease severity [6], and the use of administrative coding versus prospective data [32]. Finally, the concept of the weekend effect has recently been questioned in favor of a more complex relationship of the admission time and outcome [6]. Thus, different definitions of weekend or off-hours may explain some of the variable results.

The study by Tolvi et al. reporting a weekend effect in our center included all neurological patients admitted to the university hospital, so the two studies are not directly comparable [16]. Yet, acute stroke represents the biggest patient group at our neurological Emergency Department and is one of the neurological emergencies requiring an immediate treatment irrespective of time and day. Therefore, this patient group might be particularly susceptible to factors affecting resources and decision-making ability of health-care personnel. Demonstrating the difference in patient populations between the two studies, only 16.0% of the neurological patients in the study by Tolvi et al. were admitted on weekend [16], while the percentage was 28.0% in our study, equating the expected rate of 28.6% if admissions were evenly distributed throughout the week. This shows that the critically ill, including acute stroke patients, arrive irrespective of the day of the week, whereas in a more heterogenous patient population, the organization of health care services may lead to an uneven distribution of admissions based on case severity. In addition, it is often during weekends when the most critically-ill patients are transferred from other hospitals to a tertiary center, where comprehensive resources are available 24/7. Therefore, the reported higher mortality of neurological patients at weekends in the university hospital may have resulted from inadequate adjustment for case severity [16], which has appeared as a major contributor to the weekend effect [7,13–15,33,34]. Hence, in the current study, we adjusted our results for stroke severity.

Among the few variables predicting poorer outcome in our study were admission during the autumn and winter, which have emerged since our previous analysis [17]. The outcome disadvantage of winter onset has been previously documented [35–38] and attributed to low temperature [38,39], high respiratory disease mortality [38], and an increased burden of cardiovascular risk factors [40]. However, poorer outcome has also been reported during spring [35], which, along with summer admission, predicted better outcome in our cohort. One possible explanation is the more pleasant climate and increasing amount of light during the first months after stroke, which could encourage patients to participate in outdoors activities and thus support rehabilitation.

4.1. Strengths and limitations

The strengths of the study include the accuracy of the time stamps recorded prospectively for each patient. The functional outcome data were only missing in roughly 1% of the cases, mainly due to patients permanently residing abroad, and the percentage of missed mortality outcomes is expected to be much lower. Moreover, in contrast to most studies on the weekend effect, we assessed functional outcome in addition to mortality.

Our study accompanies the usual disadvantages of a single-center, observational study. Due to the small number of patients treated with IVT beyond 4.5 h or undergoing direct endovascular thrombectomy without preceding IVT, we did not analyze them as separate subgroups, but instead excluded these patients from the analyses. Since our cohort comprised only patients treated with IVT, we cannot conclude, whether the rate of thrombolysis differed between weekdays and weekends and whether stroke patients withheld of IVT reached equal outcomes. Yet, the similar baseline characteristics of the weekend and weekday cohorts do not support different criteria for IVT administration based on the admission time.

5. Conclusions

We found no weekend effect for acute ischemic stroke patients receiving IVT that would result in higher mortality, worse functional outcome, or higher rates of sICH. Thus, our results do not confirm the previous report of worse outcome for neurological patients admitted to our institution during weekends in acute stroke population and show that an equal quality of treatment can be provided with centralized decision-making irrespective of time or day. The fact that almost two thirds of IVT treatments are executed during non-office hours underlines the importance of local standard operating procedure and ongoing education of all persons participating in the acute stroke care.

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Declaration of Competing Interest

None.

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